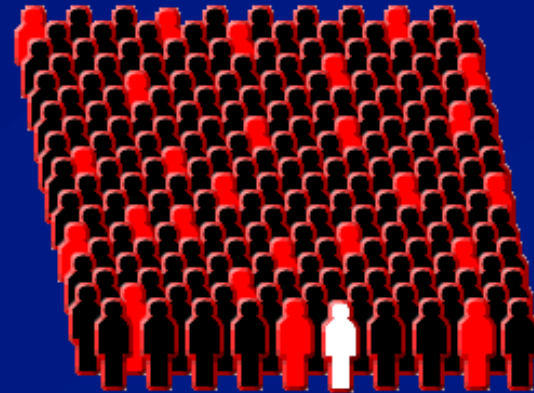
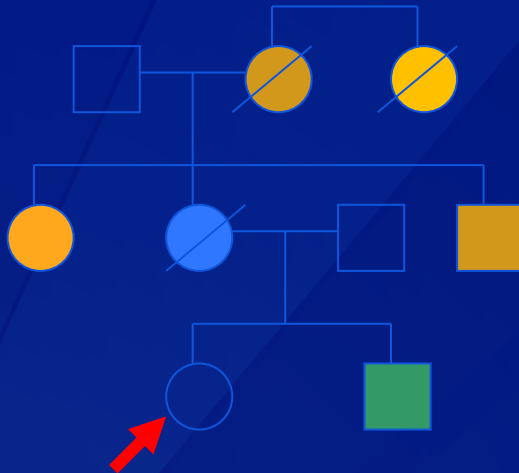


# The Importance of Family Health History In Public Health and Disease Prevention



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Office of Public Health Genomics  
Centers for Disease Control and Prevention

# Outline

- Family health history in the age of precision medicine: from genetics to genomics
- Evaluating use of family health history as a tool for public health
- Current public health efforts in using family health history for disease prevention

# Family Health History in the Age of Precision Medicine

## The Family History — More Important Than Ever

Alan E. Guttmacher, M.D., Francis S. Collins, M.D., Ph.D., and Richard H. Carmona, M.D., M.P.H.

For many observers, the term “genomic medicine” conjures up space-age images of microarray chips, bioinformatics, and designer drugs. Today, with medicine poised at the dawn of the genomic era, it is seductive to believe that such high-tech options have already become the most important genomic tools in health care. However, as so often happens

disease. Knowledge that both parents are carriers for sickle cell disease, the introduction of careful surveillance of the likelihood of disease burden. Knowledge

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in Medicine

## The family history: the first genetic test, and still useful after all those years?

Reed E. Pyeritz, MD, PhD<sup>1</sup>

The family history has its origins in genealogy and over the past century has become embedded in clinical practice. Its importance in specialized circumstances is unquestioned but largely untested. Moreover, the relevance of the family history to common diseases, especially in an era of genomic markers that convey risk and the emphasis on “personalized medicine,” must be given careful scrutiny. Given the time and expertise needed to obtain and interpret the

family history, without a clearer sense of clinical validity and utility, its role will likely diminish. The time to perform the requisite investigations is now.

*Genet Med* 2012;14(1):3–9

**Key Words:** clinical utility; family history; genealogy; genetic testing

“Abraham was the father of Isaac, Isaac the father of Jacob, Jacob the father of Judah and his brothers, Judah the father of Perez and Zerah, whose mother was Tamar, Perez the father of Hezron, Hezron the father of Ram, Ram the father of Amminadab, Amminadab the father of Nahshon, Nahshon the father of Salmon, Salmon the father of Boaz, whose mother was Rahab, Boaz the father of Obed, whose mother was Ruth, Obed the father of Jesse,

healthy females.<sup>4</sup> He documented how the family itself learned to avoid a common treatment of a variety of ailments. “So assured are the members of this family of the terrible consequences of the least wound, that they will not suffer themselves to be bled on any consideration, having lost a relation by not being able to stop the discharge occasioned by this operation.” Ten years later, Hay added the observation that unaffected daughters of affected males could themselves bear affected sons.<sup>5</sup> This information

# Family Health History for Rare Disease Diagnosis

- Rare diseases
  - < 200,000 people
  - > 7,000 rare diseases
  - 4,300 “genetic” conditions with molecular basis
- 25 million people
- “Diagnostic odyssey”
- Genome sequencing yield 25-50%
- More and more therapies found

## Family Health History “Red Flags” For Presence of Rare Genetic Disease

- Early age at onset of a common disease
- Two or more close relatives with same disorder
  - An uncommon disorder
  - A disorder known to be caused by mutation in a single gene
  - Disorders related by cause and pathogenesis, such as neoplasia
- Multifocal disease
  - Different organs
  - Paired organs
  - Multiple foci in same organ
- Disease in the less-often affected sex
- Conditions particularly common in a specific ethnic group

Pyeritz R, Genetics in Medicine, 2012

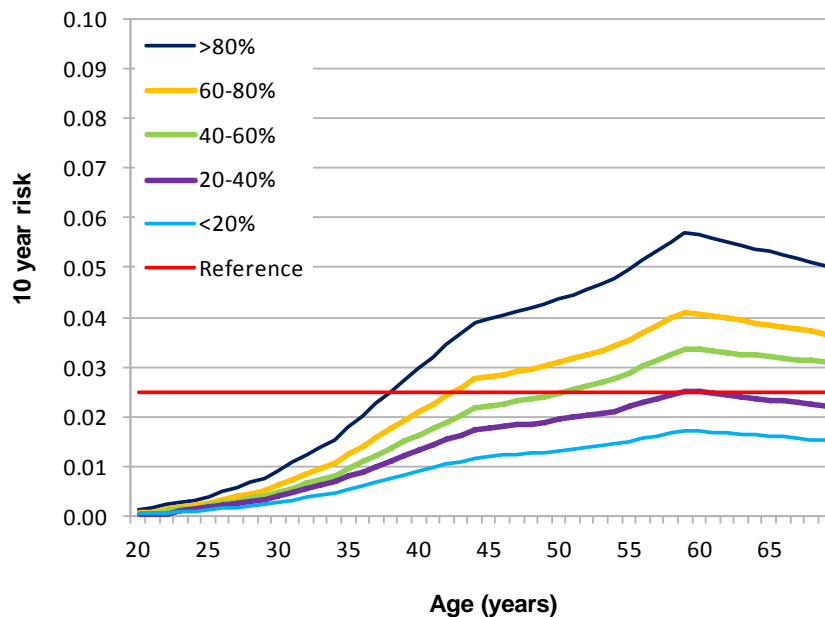
## Family Health History is a Risk Factor for Common Diseases

	Relative Risk
Heart disease	2.0 – 5.4
Breast cancer	2.1 – 3.9
Colorectal cancer	1.7 – 4.9
Prostate cancer	3.2 – 11.0
Melanoma	2.7 – 4.3
Type II diabetes	2.4 – 4.0
Osteoporosis	2.0 – 2.4
Asthma	3.0 – 7.0

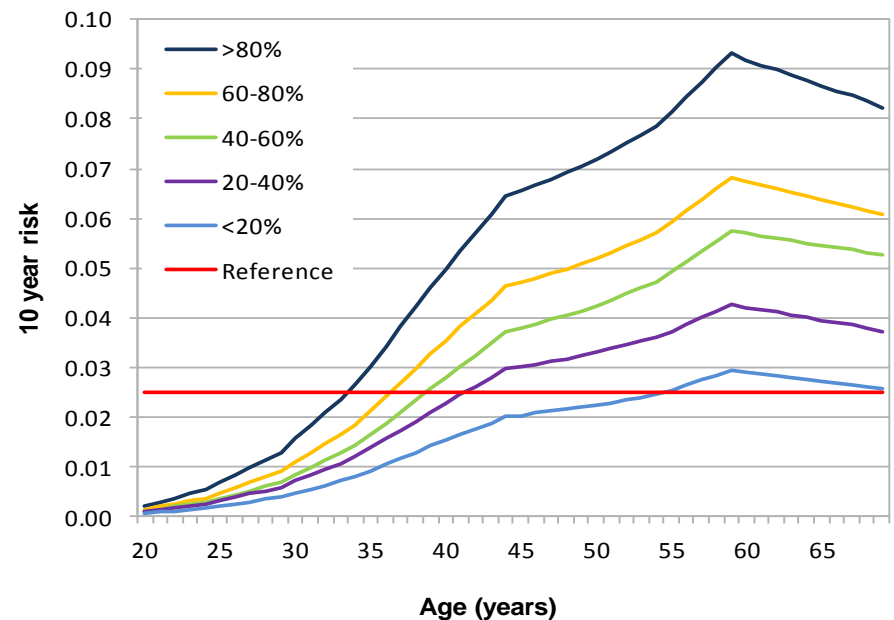
# Family Health History Adds Value to Polygenic Risk Score

## 10-year Absolute Risk of Developing Breast Cancer by polygenic risk percentiles

Women without Family History



Women with Family History



- **Reference:** 2.5% 10-year absolute risk for developing breast cancer corresponds to risk of UK women aged 47, i.e. age of invitation to the UK NHS Breast Screening programme

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## **CDC Family Healthware™ Impact Trial (FHITr)**

- Goal: To determine if personalized prevention messages tailored to familial risk motivated people at risk to change lifestyle behaviors or seek medical advice/screening
- Family Healthware™ Tool
  - Focus on coronary heart disease, stroke, diabetes, and colorectal, breast, and ovarian cancer
  - Collected information on:
    - Family health history (1<sup>st</sup> and 2<sup>nd</sup> degree relatives)
    - Health behaviors (e.g., smoking and exercise)
    - Screening tests (e.g., blood cholesterol, mammography)
  - Assessed familial risk
  - Provided personalized recommendations for lifestyle changes and screening



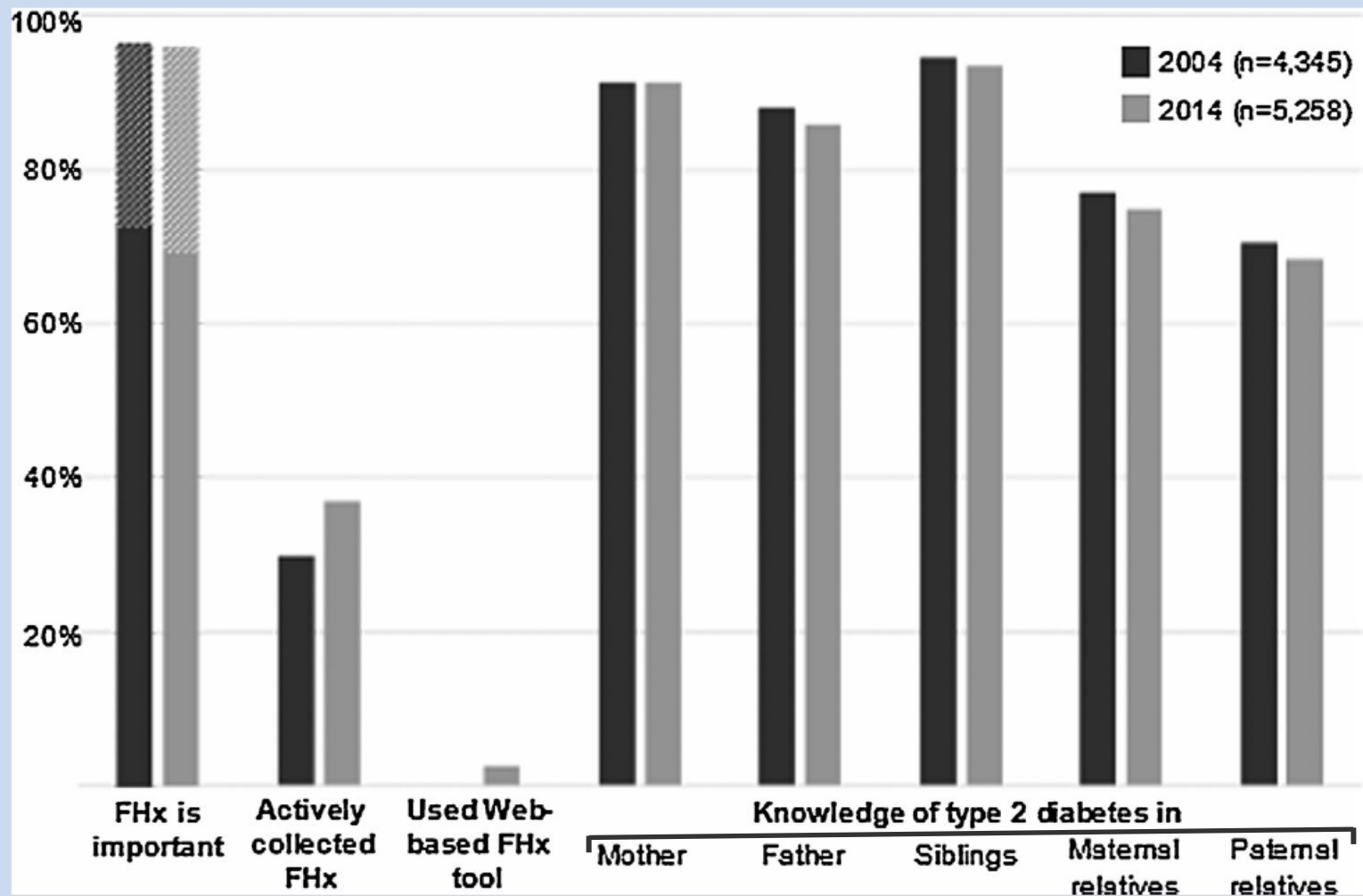
# CDC Family Healthware™ Impact Trial (FHITr)

- Cluster-Randomized Trial: compare use of Family Healthware™ vs. standard prevention messages
  - 41 primary care practices; 3786 participants,, 2105 (intervention) and 1239 i(controls) (88% completion rate)
  - Demographics: mean age 50 years, more women, high SES, health insurance and 90% non-Hispanic white
- Measured change in:
  - Risk perception (perceived risk, worry, severity, control)
  - Lifestyle behaviors (diet, exercise, smoking, alcohol use)
  - Screening behaviors (cholesterol, mammogram, colonoscopy)
  - Medical appointment seeking behaviors
  - Communication about family health history with clinician and with family
  - Referrals

## **Selected Findings from Family Healthware™ Impact Trial (FHITr)**

- 82% had strong or moderate familial risk for at least 1 disease
- Perceived risk, worry strongly associated with FHH risk
  - Highest for cancers
  - Worried most about heart disease (men), breast cancer (women)
  - Heart disease perceived to be the most controllable
  - Cancers perceived to be the least controllable
- Underreporting of paternal family history and lower perceived breast cancer risk if in the paternal lineage
- Intervention increased:
  - Daily fruit and vegetable consumption
  - Physical activity
  - Risk perceptions among those who underestimated risk
  - Communication with family among those not communicating
- Intervention decreased or had not effect on:
  - Cholesterol screening
- Automated, tailored prompts highlighting familial risk not change clinician behavior (FHH discussion, screening, referrals)

# Family History Awareness & Collection in the US: 2004 and 2014



## Many Questions Still Remain

- What is the impact of including family health history in risk assessment for disease?
- What is the impact of using family health history to guide risk-specific interventions for prevention and early detection?
- How can family health history be best used to motivate behavior change?
- Why are people not using family health history?
- How can we increase use of family health history?
- What is the best approach for reaching different target audiences with family health history messages?

How do we move from KNOWLEDGE to ACTION?

“Awareness doesn’t save lives, action does.”

-Lindsey Avner, founder and CEO of Bright Pink

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# CDC Evidence-based Classification of Family Health History Applications and Genomic Tests

<b>Tier 1</b>	<b>Supported by a base of synthesized evidence for implementation in practice</b>	<b>e.g., Family health history risk prediction for referral for BRCA genetic counseling</b>
<b>Tier 2</b>	<b>Synthesized evidence is insufficient to support routine implementation in practice; may provide information for informed decision making</b>	<b>e.g., Family health history for risk prediction for colorectal cancer screening</b>
<b>Tier 3</b>	<b>Evidence-based recommendations against use, or no relevant synthesized evidence identified; not ready for routine implementation in practice</b>	<b>e.g., Genetic testing of minors for adult-onset conditions</b>

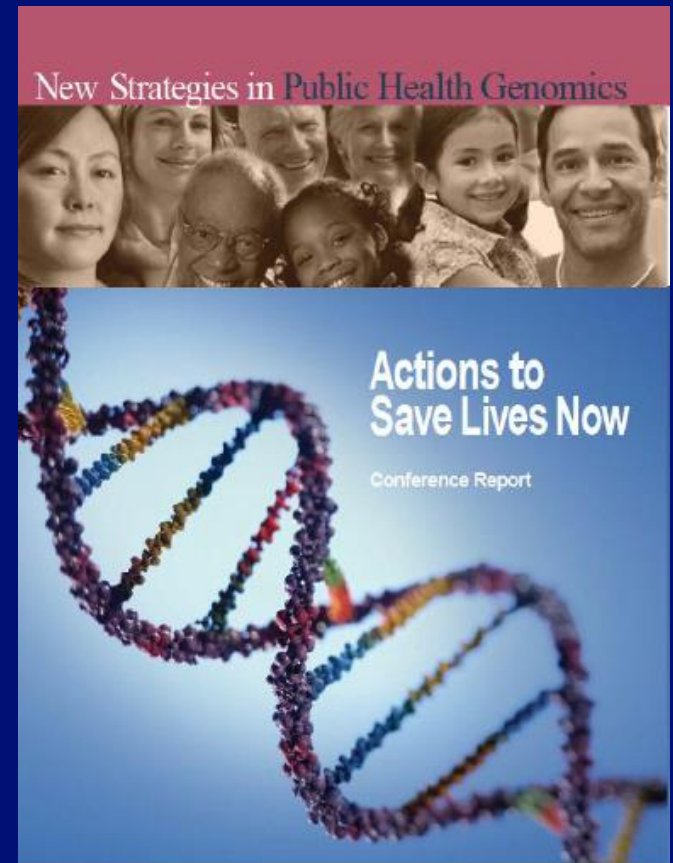
*Dotson WD, Douglas MP, Kolor K, et al. Clin Pharmacol Ther. 2014 Apr; 95(4): 394–402.*

*List of applications by level of evidence on CDC Public Health Genomics Knowledge Base website:*

*<https://phgkb.cdc.gov/GAPPKB/topicStartPage.do>*

# CDC Selected Emerging Tier 1 Genomic Applications

- Familial Hypercholesterolemia, Hereditary Breast and Ovarian Cancer, Lynch Syndrome
- 2 million people in the US
- Many don't know they have it
- Effective interventions reduce mortality
- Evidence-based recommendations
  - Familial Hypercholesterolemia
    - NICE Cascade screening
  - Hereditary Breast and Ovarian Cancer
    - USPSTF
  - Lynch Syndrome
    - EGAPP



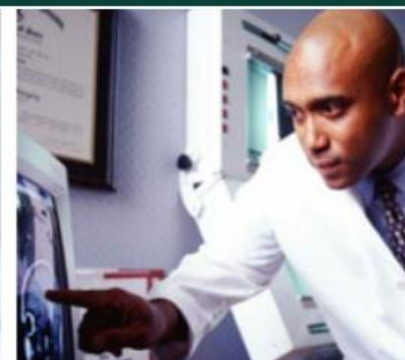
# **Tier 1 Genomic Applications Toolkit to Support Implementation in States**

- Strategies modeled on existing or past state programs:
  - Bi-directional cancer registry reporting with partner provider systems for case finding or other purposes
  - Informing policy making, such as evidence-based coverage by payers for services specified by Tier 1 recommendations
  - Developing and tracking surveillance indicators to follow progress in achieving widespread implementation of Tier 1 recommendations and the Healthy People 2020 objective
  - Designing and implementing educational outreach programs targeting the general public and health professionals with interest in Tier 1 applications
  - Cascade screening to identify the at-risk family members of index cases who can benefit from evidence-based preventive strategies
- Materials developed by states for their programs and resulting publications, as well as materials developed by CDC





## Public Health Grand Rounds



### Cancer and Family History: Using Genomics for Prevention



**Tuesday, April 19, 2016 at 1 pm EDT**

The risk factors for cancer are many and varied, and inherited genetic mutations play a major role in 5 to 10% of all cancers. When these mutations are identified early, patients are able to work with their healthcare providers to take crucial steps toward care and treatment. Many of those affected by genetic cancer syndromes don't know that genetic testing is an option.

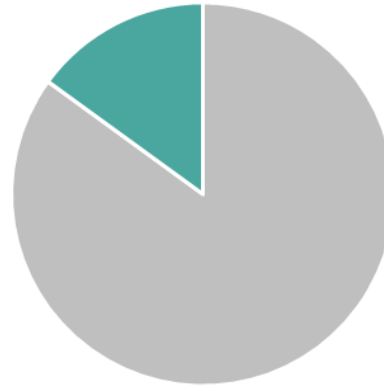


# Hereditary Breast and Ovarian Cancer (HBOC) Syndrome

- Involves mainly mutations to tumor suppressor genes
  - *BRCA1* or *BRCA2*
- Associated with increased risks for breast, ovarian, prostate, and pancreatic cancers
- About 1 in every 500 women in the U.S. has a mutation in either the *BRCA1* or *BRCA2* genes



**Up to 10%** or approximately  
**22,000** cases of  
breast cancer each year



**15%** or approximately  
**3,000** cases of  
ovarian cancer each year

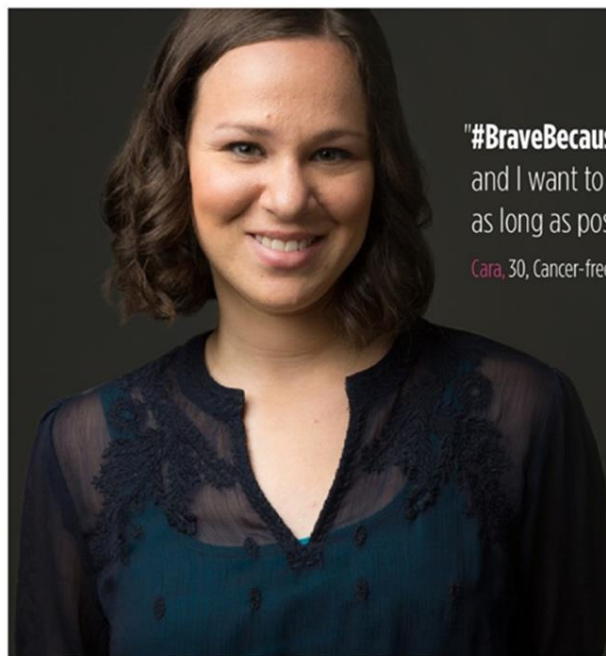


An interactive web  
resource with unique areas  
for consumers and  
healthcare providers

Launched on May 8, 2014

**Know:BRCA**

KNOWING YOUR BRCA GENE MUTATION RISK CAN SAVE YOUR LIFE



"#BraveBecause life is an amazing gift  
and I want to make sure I can enjoy it  
as long as possible!"

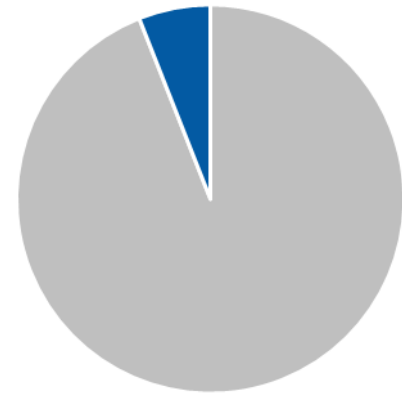
Cara, 30, Cancer-free since 2011



Share your story on Facebook and Twitter  
using #BraveBecause to inspire other  
young women to understand their breast  
cancer risk.

## Lynch Syndrome

- Involves mutations in mismatch repair genes, which lead to tumors with microsatellite instability
- Associated with increased risks for colorectal, endometrial, ovarian, stomach cancers and other types of cancer



**Up to 3% or approximately  
4,000 cases of  
colorectal cancer each year**



## Have You or a Family Member Had Colorectal (Colon) Cancer?



Language: English



Having a family health history of colorectal (colon) cancer can make you more likely to get colorectal cancer yourself. If you have close family members with colorectal cancer, collect your family health history of colorectal and other cancers, and share this information with your doctor. If you have had colorectal cancer, make sure that your family members know about your diagnosis, especially if you have Lynch syndrome.

### Why is it Important to Know Your Family Health History?



# Hereditary Cancers: Personal Stories

*Over 1 million people in the United States have an increased risk for certain types of cancer because they have Hereditary Breast and Ovarian Cancer Syndrome (HBOC) or Lynch syndrome. HBOC is a condition that increases a person's chance*

[Show more](#)



# Familial Hypercholesterolemia Associated with Preventable Premature Heart Disease

- Involves mutations in the low-density lipoprotein (LDL) receptor gene
- Associated with high cholesterol levels (from birth) and can lead to early development of coronary heart disease (CHD) or atherosclerosis
- Lifestyle changes, including changes in diet and exercise, are highly recommended in patients with FH
- Lipid-lowering drug therapy is usually also needed in adult patients and more intensive therapy may also be required
- Prevalence estimated between 1:200 and 1:500





## Treatment Gaps in Familial Hypercholesterolemia

- >1,200 patients from the FH CASCADE Registry
- Median age at initiation of lipid-lowering therapy = 39 years
- Median age at FH diagnosis = 47 years
- Prevalent coronary heart disease reported in 36% of patients
- More than half of patients did not achieve adequate LDL-C lowering



## Does Heart Disease Run in Your Family?



Language: English



If you have family members with heart disease, you might be more likely to develop heart disease yourself. Take time to collect your family health history information and share this information with your doctor and other family members. Your doctor can help you take steps to lower your chances of getting heart disease.

Collect and Share Your Family Health History of Heart Disease



## Summary

- Family history in the age of precision medicine: from genetics to genomics
  - More important than ever
- Evaluating use of family history as a tool for public health
  - FH has added value to existing disease prevention efforts but many questions remain
- Current public health efforts in using family history for disease prevention
  - Need to ramp up collaborative efforts!